Testimony
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Subcommittee on National Security, Emerging Threats, and International Relations
United States House of Representatives

Examining VA Implementation of the Persian Gulf War Veterans Act of 1998

Statement of

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Mr. Chairman and members of the Subcommittee, my name is James O'Callaghan. I head the Molecular Neurotoxicology Laboratory at the National Institute for Occupational Safety and Health (NIOSH), and I was recently appointed to serve on the Department of Veterans Affairs (VA) Research Advisory Committee on Gulf War Veterans' Illnesses. I am pleased to be here in my capacity as a member of the Advisory Committee to discuss the use of data from animal studies to diagnose and treat human brain disorders.

Over the past 25 years I have focused my research on detecting and characterizing the adverse effects of chemicals and drugs on the nervous system – research that includes the use of experimental animals to model human brain damage. In biomedical research, investigations using animal models are useful for understanding disease processes and for the development of relevant therapies for brain disorders that afflict humans. The use of animal models is useful in neurosciences because, short of obtaining post-mortem brain samples at autopsy, there is no other way to discover and understand the basis of brain disorders. Moreover, while one might expect that brain disorders and brain damage may be easily detected in the living human using psychiatric and neurological examinations, or even "state of the art" imaging, such is generally not the case. Think for a moment of the two devastating diseases of the human nervous system, Alzheimer's disease and Parkinson's disease. We can diagnose these distinct brain disorders in the living human, but, these are progressive neurological diseases that result from underlying brain damage that starts decades earlier. It is estimated that it takes the loss of 70-80% of the neurons affected in Parkinson's disease before the onset of clinical symptoms can be detected.

This means that one is suffering from the disease long before symptoms are evident. Thus, as neuroscientists, we are faced with the problem of having evidence of end stage disease without knowing the cause or even milestones of disease progression. This is where animal models are so useful. For example, genetically engineered mice and mice treated with selective neurotoxins now make it possible to replicate features of diseases such as Parkinson's and Alzheimer's in a controlled laboratory setting. These advances raise hope for a better understanding of the molecular basis of these debilitating diseases and for the eventual introduction of therapies before symptoms become manifest and before the disease process has advanced. Such research and interventions are especially useful to NIOSH's work to enhance worker safety and health since excess neurodegenerative disease, including Parkinson's and Alzheimer's, has been associated with a variety of occupations and workplace exposures.

Although animal studies can be quite useful, they do have limitations. The major weakness of such studies is that biological differences between humans and animals may result in different responses to neurotoxins or medical interventions. So it is important to bear in mind that animal data are not always predictive of human responses. When available, scientifically sound epidemiological data – data that are based on the study of the distribution and determinants of disease in human populations – are superior to animal data. However, in cases where information about human exposure is lacking, research in a controlled experimental setting, generally using animals, can provide useful scientific information.

Animal models not only hold promise for leading to cures for neurological diseases, they form the cornerstone for safety assessments and have proven to have predictive validity for setting margins of safety for potential adverse effects of drugs, including adverse effects on the nervous system. Animal data have been used to help establish the margins of safety to protect humans from drug-induced toxicity, to set pesticide exposure limits, and to determine if specific agents or mixtures have the potential for adverse long-term outcomes. As the relationship between chronic, low-level exposures and adverse neurological outcomes has become better understood, the Department of Veterans Affairs and the U.S. Army have established animal research programs to further our understanding of the relationship between chemical exposures and neurodegenerative diseases. The long-term goals of these programs are to relate short- and long-term exposures to specific chemical agents and mixtures to the development of brain disorders and to develop specific neuroprotective agents and strategies to protect against the development of nervous system disorders. In summary, animal studies have been, and will continue to be, of great importance in establishing a predictive relationship between specific exposures in humans and subsequent adverse effects on the nervous system.

Again, thank you for the opportunity to testify before you today. I would be happy to answer any questions you may have.